

## 90S Abstracts

induced atherosclerotic change characterized by the histologic presence of foamy macrophages and cholesterol clefts had been fully attenuated by the chronic presence of everolimus.

**Conclusions:** In this experimental animal model, long-term local arterial stent-mediated delivery of everolimus inhibited the formation of early neointimal hyperplasia and atherosclerosis.

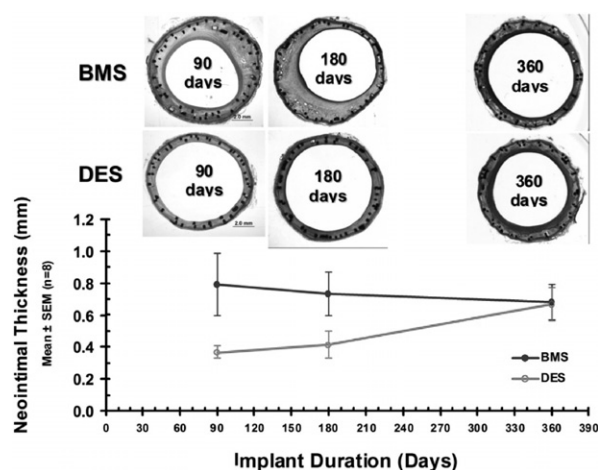


Fig. 1. Measurement of neointimal thickness (mm) by histomorphometry and representative images for BMS and DES at 3, 6 and 12 months post-implantation.

**Author Disclosures:** A. Nikanorov: Abbott Vascular, Employment (full or part-time); L. B. Schwartz: Abbott Laboratories, Employment (full or part-time); R. Virmani: Abbott Vascular, Consulting fees or other remuneration (payment); H. Zhao: Abbott Vascular, Employment (full or part-time).

## PS234.

### Edaravone Suppresses Reperfusion Injury following Leg Ischemia in Rats: Transmission Electro Microscopic Study

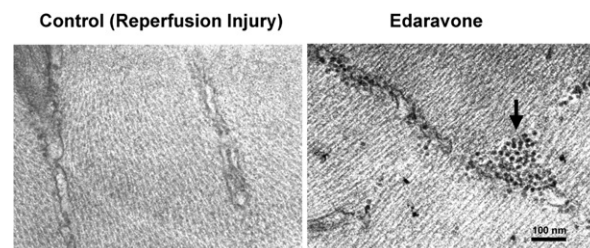
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**Objectives:** It is well known that free radicals cause reperfusion injury after leg ischemia. At Vascular Annual Meeting 2010, our pathohistological study of Periodic Acid Schiff staining showed that the free-radical scavenger, edaravone (Radicut®, Mitsubishi Tanabe Pharma Co., Japan) suppressed reperfusion injury and maintained high glycogen stores in lower extremity muscles. In the present study, we used transmission electro microscope (TEM) to elucidate how edaravone suppresses reperfusion injury.

**Methods:** Male Lewis rats ( $632 \pm 89$  gm) were intraperitoneally injected with edaravone (3.0 mg/kg, edaravone group,  $n = 3$ ) or the same dose of saline (control group,  $n = 3$ ). Reperfusion injury models were induced by clamping bilateral common femoral arteries for 5 hours and then de-clamping. At least 5 hours after reperfusion, the transverse sections of lower extremity muscles were immediately made using a diamond knife. Under a TEM (JEM-1220, Nippon Denshi Co., Japan), we counted the number of glycogen-granules at 50,000x magnification on each 5 different fields.

**Results:** The TEM sections from the control group showed marked loss of glycogen-granules with swollen mitochondria. In contrast, the TEM sections from the edaravone group showed numerous glycogen-granules and normal mitochondria (Figure). The mean density of glycogen-granules in the edaravone group was significantly higher than that in the control group ( $88.6 \pm 5.4$  vs.  $11.6 \pm 3.0$  particles/ $\mu m^2$ ,  $p < 0.001$ ).

**Conclusions:** Our TEM results confirmed that edaravone suppresses reperfusion injury following leg ischemia by maintaining the glycogen-granules in muscles.



**Author Disclosures:** S. Fukui: Nothing to disclose; M. Mitsuno: Nothing to disclose; Y. Miyamoto: Nothing to disclose; M. Ryomoto: Nothing to disclose; H. Tanaka: Nothing to disclose; M. Yamamura: Grant-in Aid for Researchers, Hyogo College of Medicine 2010, Research Grants; Y. Yoshioka: Nothing to disclose.

## PS236.

### Hyperglycemia-Induced Adult Dermal Fibroblast Dysfunction

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**Objectives:** Dermal fibroblasts are key cells in wound healing and remodeling by secreting MMP-2, MMP-9 and TGF- $\beta$ . Patients with metabolic syndrome and diabetes with subsequent hyperglycemia are at increased risk of impaired wound healing. Although the effects of hyperglycemia are well characterized in many different tissues, little is known about the effects on dermal fibroblast function. We hypothesize that hyperglycemia causes decreased rates of proliferation and MMP-2, MMP-9 and TGF- $\beta$  secretion.

tion, consistent with the phenotype of fibroblasts found in non-healing wounds.

**Methods:** Commercially available adult dermal fibroblasts were grown in physiologic glucose concentrations (PGC), serum starved (24 h), then exposed to either PGC (5.5 mM), or hyperglycemic glucose concentration (HGC) (25 mM) and evaluated at 24 and 48 hours. Cellular proliferation was determined by PCNA expression and MTT assay and conditioned media was analyzed for TGF- $\beta$  secretion or MMP-2 and MMP-9 activity, by ELISA or gel zymography, respectively.

**Results:** HGC resulted in significantly decreased proliferation as measured by MTT assay when compared to PGC after both 24 and 48-hours. HGC resulted in a significantly decreased proliferation as determined by PCNA expression at 48 hours when compared to PGC ( $178,113 \pm 86,068$  vs.  $386,579 \pm 99,123$  AU,  $P=0.004$ ,  $n=3$ ). TGF- $\beta$  secretion was significantly decreased by HGC at the 24-hour time point when compared to PGC ( $1606 \pm 313$  vs.  $2341 \pm 345$  pg/ml,  $P=0.02$ ,  $n=3$ ). While, no differences were observed in MMP-9 activity from hyperglycemic media, there was a significant decrease in MMP-2 activity, after 48 hours, in the conditioned media from cells exposed to HGC when compared to PGC controls.

**Conclusions:** These results suggest that hyperglycemic conditions of metabolic syndrome and diabetes may contribute, in part, to the development of venous ulcers and non-healing wounds by the inhibition of fibroblast proliferation and MMP-2 and TGF $\beta$  secretion.

**Author Disclosures:** J. P. Cullen: Nothing to disclose; A. J. Doyle: Nothing to disclose; D. Gillespie: Nothing to disclose; E. Roztocil: Nothing to disclose.

#### PS238.

##### **Multisystem Trauma Patients with Venous Thromboembolism have Increased Circulating Microparticles**

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**Objectives:** Multisystem trauma incurs significant venous thromboembolism (VTE) risk. Membrane-shed circulating annexin V+ microparticles (MPs) carrying tissue factor (TF) are released from activated cells and implicated in cancer-associated thrombosis. The objective of this study is to quantitate circulating MPs in trauma patients with and without VTE, in order to identify a role for circulating MPs in trauma-related thrombosis.

**Methods:** Plasma was obtained from patients admitted to the trauma ICU based upon pre-existing criteria and from healthy volunteers according to an IRB-approved protocol. Plasma was incubated with annexin V+ and MPs analyzed using FACS.

**Results:** Of the patients studied ( $n=10$ ), trauma patients with VTE had more circulating annexin V+ MPs

(2018.3 MPs per ul) than did trauma patients without VTE (874.7 MPs per ul). All trauma patients had increased circulating annexin-V+ MPs compared to their matched controls (Fig. 1).

**Conclusions:** Our preliminary data demonstrate that multisystem trauma patients who develop VTE have increased circulating annexin V+ MPs, suggesting a role for MPs in trauma-related VTE. Our ongoing investigation will potentially lead to the identification of novel VTE risk biomarkers and new anticoagulation targets.

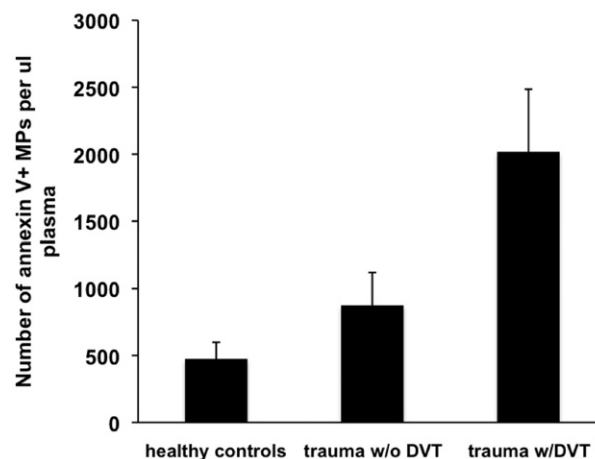


Figure 1. Trauma patients with DVTs have increased circulating annexin V+ MPs. A. Number of annexin V microparticles per ul of plasma in healthy controls ( $n=5$ ), trauma patients w/o DVT ( $n=5$ ) and trauma patients w/DVT ( $n=3$ ).

**Author Disclosures:** D. Gillespie: Nothing to disclose; M. Mathews: Nothing to disclose.

#### PS240.

##### **Pathophysiologic Correlation of Fat Emboli Load during Medullary Canal Pressurization: The Effect of Temporary Intravenous Filtration**

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**Objectives:** Patients with femoral shaft fractures treated with intramedullary nailing (IMN) are at increased risk for pulmonary fat embolization. The purpose of this study was to: 1) demonstrate the ability of retrievable filters to capture medullary debris 2) evaluate how filtration affects cardiovascular physiology after IMN and 3) evaluate lung pathology to determine whether filtration affects fat emboli load.

**Methods:** Canines were anesthetized and hemodynamic monitoring established. Carotid embolic protection filters were introduced into the iliac vein and ipsilateral intramedullary reaming and nailing was performed. Control group (4) was compared to groups treated with Accu-